Infections Complicating the Care of Combat Casualties During Operations Iraqi Freedom and Enduring Freedom

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Background: Continued assessment of casualty complications, such as infections, enables the development of evidence-based guidelines to mitigate excess morbidity and mortality. We examine the Joint Theater Trauma Registry (JTTR) for infections and potential risk factors, such as transfusions, among Iraq and Afghanistan trauma patients.

Methods: JTTR entries from deployment-related injuries with completed records between March 19, 2003, and April 13, 2009, were evaluated using International Classification of Diseases-9 codes for infections defined by anatomic/clinical syndromes and/or type of infecting organisms. Risk factors included mechanisms of injury, patient demographics, Injury Severity Score (ISS), and transfusion, including massive transfusions (≥10 units of packed red blood cells).

Results: We reviewed 16,742 patients entries (15,021 from Operation Iraqi Freedom (9,883 battle injuries [BI]) and 1,721 from Operation Enduring Freedom (1,090 BI). A total of 96.6% were men and 77.6% were Army personnel. The majority of BI were due to explosive devices (36.3%). There were 921 patients (5.5%) who had one or more infection codes with only 111 (0.6%) recorded deaths (16 with infections). Infections were commonly gram-negative bacteria (47.6%) involving skin/wound infections (26.7%), and lung infections (14.6%). Risk factors or associations that were most notable in univariate and multivariate analysis were calendar year of trauma, ISS, and pattern of injury.

Conclusion: The 5.5% infection rate is consistent with previous military and civilian trauma literature; however, with the limitations of the JTTR, the infection rate is likely an underrepresentation due to inadequate level V and long-term infectious complications data. Combat operational trauma is primarily associated with gram-negative bacteria typically involving infections of wounds or other skin structures and lung infections such as pneumonia. They are commonly linked with higher ISS and injuries to the head, neck, and face.

Key Words: Combat, Infection, Afghanistan, War, Trauma registry.

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Infectious complications are primary causes of morbidity among patients that suffer combat- and noncombat-related trauma and are a leading cause of mortality in patients who survive the first few days after injury.[1–9] A recent review of noncombat trauma patients admitted to a military trauma center revealed that 8.2% of 4,566 trauma patients developed an infection.[10] In that study, infected trauma patients had higher mortality, and greater number of hospital days and days spent in the intensive care unit (ICU). In addition, the role of infection control in preventing infectious complications was addressed, which has become a major area of emphasis within the combat operations in Iraq and Afghanistan.[10–12]

A primary focus to improve trauma care has been the use of trauma systems or registries, which have been implemented in the military with the Joint Theater Trauma System (JTTS) and the Joint Theater Trauma Registry (JTTR).[13] The US Department of Defense (DoD) in collaboration with the US Army Institute of Surgical Research has developed numerous evidence-based clinical practice guidelines within the JTTS, which have reportedly decreased postinjury complications by 54% although no infection outcome data has been described.[14] There are currently 31 JTTS clinical practice guidelines (http://www.usaisr.amedd.army.mil/cpgs.html, accessed July 24, 2010) focusing on trauma care. There are some infectious disease–specific clinical practice guidelines including those with recommendations for antibiotics and casualty decolonization, ventilator-associated pneumonia treatment, and postsplenectomy vaccination. To establish clear evidence-based recommendations, system wide and patient specific data are required; however, most combat-related injury infection studies are small, single facility, single injury pattern descriptions.[5,15–23] Only one systematic review of infectious complications associated with trauma-related injuries in Iraq and Afghanistan has been performed using the JTTR, but this study had numerous limitations including the years the study spanned the total number of

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patients, risk factors included, and definitions of infection.[24] Overall, many of the evidence-based clinical practice guidelines, including the infection specific guidelines, have limited level of evidence for the recommendations. This can substantially influence the quality of the recommendations. Ongoing studies of infections in the combat zone are required to mitigate excess morbidity and mortality from combat-related injury infections. This study expands on the previous review of infections associated with trauma to include a larger population of JTTR entries, a broader array of risk factors, including transfusion data, hospital and ICU length of stays, and days of mechanical ventilation, and more complete records on the length of posttrauma follow-up recorded in the JTTR. This should allow for adjustments for individual patients' time at risk for trauma-associated infectious complications.

MATERIALS AND METHODS

The JTTR is a DoD performance improvement program that collects medical data from patients suffering combat- and noncombat-related trauma during military operations in Iraq and Afghanistan. The JTTR contains data that are collected and tabulated in a central repository database. Although some data are available from the point of injury, the majority of the data are collected at Level III (NATO Role 3) medical facilities, such as combat support hospitals, and through the various levels of medical care until reaching definitive medical care at US military treatment facilities. There has been an unavoidable lag in completion of records, which not only motivates our current analysis as an update to the previous review,[24] but it also underscores the need to carefully consider how recent years' data may be limited. This study was reviewed and approved by the Brooke Army Medical Center Institutional Review Board and the scientific review boards of the Unites States Army Institute of Surgical Research and the Infectious Disease Clinical Research Program.

This study assessed the JTTR for the presence of infections associated with trauma sustained during combat operations in Iraq and Afghanistan. Data recovery from the JTTR for use in this study included patients with completed records between March 19, 2003, and April 13, 2009. The data collected included summary totals of patients with data captured in the JTTR by year and theater of operation, with associated age, gender, military rank, branch of military service, Injury Severity Score (ISS), medical care level at the time of diagnosis (Level I, II, III, IV, and V), battle injuries (BI) or non-BI, injury site(s), Glasgow Coma Scale (GCS), and mechanism(s) of injury. Other variables included transfused blood products along with the receipt of massive transfusion (defined as 10 or more units of packed red blood cells (PRBCs) or whole blood during the first 24 hours after injury), duration of hospitalization, duration of ICU stay, and duration of mechanical ventilation. Injury patterns were grouped by anatomic distribution, which were determined by the presence of 1 or more non-zero ordinal scores specific to that body region within the Military Abbreviated Injury Scale (MAIS). MAIS body regions were grouped accordingly: head/neck, face, thorax, including injury to spine; abdomen, including injury to pelvic contents; extremity injury, whether upper or lower; and external injury, including burns and other trauma. Infectious complications were captured using International Classification of Diseases (ICD)-9 codes entered within the JTTR. The infectious complications were bundled for analysis based upon major categories of anatomic/clinical syndromes, which included bacteremia, abdominal, bone/joint, skin, lung, urine, central nervous system and other. Infectious disease ICD-9 codes were also bundled into gram-positive bacteria, gram-negative bacteria, other bacteria, and fungi.

Statistical analysis included descriptive evaluation of various subgroups of the overall cohort, point, and interval estimates for standard logistic and Poisson regression coefficients within multivariate analyses, whereas univariate or bivariate analyses included the unpaired Student's t test or Wilcoxon Mann-Whitney rank-sum test for continuous variables, and χ^2 or Fisher's exact test for categorical variables where appropriate. A nominal 0.05 significance level was used throughout these analyses. Association analyses included logistic regression to yield estimates comparable with results from the previous review of available JTTR data,[24] whereas the more complete set of records available for the current review allowed greater precision by adjusting for individual differences in length of posttrauma hospitalization. Multivariate analyses are expanded here to employ an outcome of counts of infectious complications, modeled with

TABLE 1. Total Number of Individual Recorded Diagnosis/Procedure Codes by Trauma and Infections Reviewed From the JTTR for OIF and OEF

		Patients With ICD-9 Codes by Year of Trauma and Infections							
Combat Zone	**Number of Patients**	**Total**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
OIF/OEF	16,742	6,277 (129)	3,503 (82)	3,975 (97)	3,752 (86)	3,465 (36)	3,297 (24)	2,518 (6)	1,146 (0)
OIF	15,021	6,114 (127)	3,453 (80)	3,926 (95)	3,678 (83)	3,372 (35)	3,132 (24)	2,218 (6)	855 (0)
Battle injuries	9,883	5,474 (116)	2,643 (67)	3,567 (89)	3,385 (78)	3,102 (29)	2,873 (19)	1,885 (4)	623 (0)
Non-battle injuries	4,971	3,928 (76)	2,332 (51)	1,989 (44)	1,851 (29)	1,586 (14)	1,401 (6)	1,339 (3)	487 (0)
OEF	1,721	2,981 (41)	752 (16)	1,010 (16)	1,188 (17)	1,315 (6)	1,373 (0)	1,600 (1)	704 (0)
Battle injuries	1,090	2,557 (35)	455 (14)	759 (15)	910 (13)	991 (4)	1,137 (0)	1,496 (1)	629 (0)
Non-battle injuries	599	1,604 (10)	410 (1)	437 (1)	529 (7)	663 (3)	614 (0)	490 (0)	202 (0)

Values given in parentheses are number of infections.

TABLE 2. Patient Demographics in the JTTR for Casualties of OIF and OEF

	Total	2003	2004	2005	2006	2007	2008	2009
Number of patients	16,742	2,703	3,500	2,561	2,711	3,047	1,883	337
Gender, n (%)								
Female	561 (3.4)	144 (5.3)	115 (3.3)	81 (3.2)	66 (2.4)	87 (2.9)	55 (2.9)	13 (3.9)
Male	16,178 (90.6)	2,559 (94.7)	3,385 (96.7)	2,477 (96.7)	2,645 (97.6)	2,960 (97.1)	1,828 (97.1)	324 (96.1)
Unknown	3 (0.0)	0 (0.0)	0 (0.0)	3 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Branch of service, n (%)								
Army	12,995 (77.6)	2,371 (87.7)	2,396 (68.5)	1,877 (73.3)	1,987 (73.3)	2,543 (83.5)	1,543 (81.9)	278 (82.5)
Marine	2,991 (17.9)	262 (9.7)	940 (26.9)	569 (22.2)	569 (21.0)	380 (12.5)	232 (12.3)	39 (11.6)
Air force	374 (2.2)	37 (1.4)	75 (2.1)	59 (2.3)	66 (2.4)	72 (2.4)	52 (2.8)	13 (3.9)
Navy	382 (2.3)	33 (1.2)	89 (2.5)	56 (2.2)	89 (3.3)	52 (1.7)	56 (3.0)	7 (2.1)
Military grade/rank, n (%)								
Enlisted	15,508 (92.6)	2,493 (92.2)	3,266 (93.3)	2,371 (92.6)	2,535 (93.5)	2,822 (92.6)	1,710 (90.8)	311 (92.3)
Warrant	11 (0.7)	31 (1.1)	20 (0.6)	14 (0.5)	12 (0.4)	21 (0.7)	20 (1.1)	1 (0.3)
Officer	1,005 (6.0)	159 (5.9)	195 (5.6)	154 (6.0)	159 (5.9)	194 (6.4)	120 (6.4)	24 (7.1)
Unknown	110 (0.7)	20 (0.7)	19 (0.5)	22 (0.9)	5 (0.2)	10 (0.3)	33 (1.8)	1 (0.3)
Disposition, n (%)								
Alive	16,631 (99.3)	2,681 (99.2)	3,459 (98.8)	2,545 (99.4)	2,692 (99.3)	3,038 (99.7)	1,881 (99.9)	335 (99.4)
Dead	111 (0.7)	22 (0.8)	41 (1.2)	16 (0.6)	19 (0.7)	9 (0.3)	2 (0.1)	2 (0.6)
Total OIF, n (%)								
OIF	15,021 (89.7)	2,575 (95.3)	3,344 (95.5)	2,377 (92.8)	2,402 (88.6)	2,645 (86.8)	1,420 (75.4)	258 (76.6)
Battle injury	9,883 (65.8)	1,085 (42.1)	2,381 (71.2)	1,734 (72.9)	1,822 (75.9)	2,029 (76.7)	719 (50.6)	113 (43.8)
Total OEF, n (%)								
OEF	1,721 (10.3)	128 (4.7)	156 (4.5)	184 (7.2)	309 (11.4)	402 (13.2)	463 (24.6)	79 (23.4)
Battle injury	1,090 (63.3)	46 (35.9)	78 (50.0)	91 (49.5)	174 (56.3)	286 (71.1)	360 (77.8)	55 (69.6)
GCS								
Mean (range), N = 13,435	13.4 (3–15)	14.2 (3–15)	13.5 (3–15)	12.7 (3–15)	13.0 (3–15)	13.6 (3–15)	13.9 (3–15)	13.9 (3–15)
ISS								
MAIS, N	16,739	2,700	3,500	2,561	2,711	3,047	1,883	337
MAIS, mean (range)	10.2 (0–75)	6.2 (0–75)	10.1 (1–75)	12.0 (1–75)	12.5 (1–75)	11.4 (1–75)	8.7 (1–75)	8.7 (1–75)
ISS2005, N	16,739	2,700	3,500	2,561	2,711	3,047	1,883	337
ISS2005, mean (range)	7.8 (0–75)	5.0 (0–75)	7.4 (1–75)	9.1 (1–75)	9.1 (1–75)	8.7 (1–75)	7.1 (1–75)	7.3 (1–75)
MAIS								
Head/neck, mean (range)	2.6 (1–6)	2.5 (1–6)	3.4 (1–6)	3.1 (1–6)	2.3 (1–6)	2.2 (1–6)	2.0 (1–6)	2.3 (1–6)
Face, mean (range)	1.5 (1–6)	1.3 (1–5)	1.5 (1–5)	1.5 (1–5)	1.5 (1–5)	1.5 (1–5)	1.5 (1–5)	1.6 (1–6)
Thorax, mean (range)	2.8 (1–6)	2.6 (1–5)	2.8 (1–6)	2.8 (1–6)	2.8 (1–6)	2.8 (1–5)	2.6 (1–6)	2.6 (1–6)
Abdomen, mean (range)	2.4 (1–6)	2.0 (1–5)	2.4 (1–5)	2.5 (1–5)	2.5 (1–6)	2.5 (1–5)	2.3 (1–5)	2.4 (1–5)
Extremities, mean (range)	2.4 (1–6)	2.1 (1–5)	2.4 (1–6)	2.5 (1–6)	2.5 (1–6)	2.6 (1–5)	2.3 (1–5)	2.2 (1–6)

TABLE 2. Patient Demographics in the JTTR for Casualties of OIF and OEF (continued)

	Total	2003	2004	2005	2006	2007	2008	2009
External, mean (range)	1.2 (1–6)	1.1 (1–5)	1.2 (1–6)	1.3 (1–6)	1.3 (1–6)	1.3 (1–6)	1.2 (1–6)	1.2 (1–5)
Hospital days, median (range), N = 16,587	4 (0–2196)	4 (0–2196)	5 (0–1107)	5 (1–1524)	4 (1–1099)	3 (0–759)	2 (1–366)	2 (1–157)
Ventilator days, median (range) N = 15,912	0 (0–405)	0 (0–34)	0 (0–75)	0 (0–405)	0 (0–87)	0 (0–97)	0 (0–36)	0 (0–43)
Days in the ICU, median (range) N = 16,062	1 (0–337)	1 (0–220)	1 (0–37)	1 (0–103)	1 (0–87)	0 (0–23)	0 (0–204)	0 (0–49)
Massive transfusion, number of patients	768	32	132	149	183	180	83	9
Whole blood, median (range)	0 (0–56)	0 (0–20)	0 (0–27)	0 (0–38)	0 (0–44)	0 (0–56)	0 (0–16)	0 (0–20)
Red blood cell, median (range)	6 (0–74)	5 (0–22)	5 (0–41)	5 (0–69)	6 (0–70)	7 (0–66)	7 (1–74)	8 (1–34)
Platelet, median (range)	0 (0–34)	0 (0–0)	0 (0–4)	0 (0–34)	0 (0–19)	0 (0–16)	0 (0–20)	0 (0–4)
Cryoprecipitate, median (range)	0 (0–13)	0 (0–0)	0 (0–7)	0 (0–11)	0 (0–7)	0 (0–13)	0 (0–6)	0 (0–5)
Fresh frozen plasma, median (range)	4 (0–82)	0 (0–18)	1 (0–33)	3 (0–47)	4 (0–61)	5 (0–82)	5 (0–62)	6 (0–20)
Red blood cell + whole blood, median (range)	6 (0–107)	5 (0–35)	6 (0–66)	5 (1–107)	6 (1–97)	8 (1–105)	7 (1–74)	8 (1–54)
Infectious events*, 1 or more	921 (5.5)	220 (8.1)	319 (9.1)	278 (10.9)	62 (2.3)	30 (1.0)	12 (0.6)	0 (0.0)

Massive transfusion, defined as 10 or more units of blood product support.
* Possible underreporting due to limitations described in the discussion section.

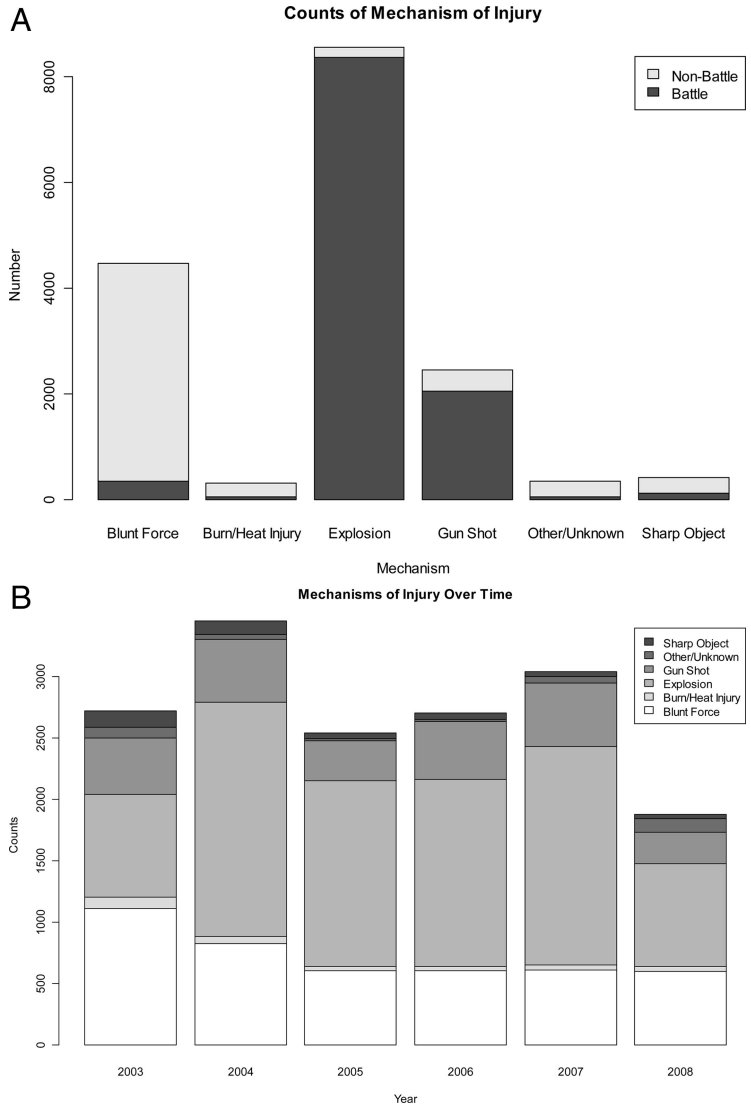

Figure 1. (*A*) Number of patients by mechanism of injury. (*B*) Distribution of trauma over time.

TABLE 3. Infection ICD-9 Coding Based on Anatomical/Clinical Syndrome or Pathogen Bundled*

	Syndrome	Total	2003	2004	2005	2006	2007	2008	2009
Anatomical and clinical syndrome	Abdomen	61	11	28	13	6	2	1	0
	Bacteremia	111	27	44	36	2	2	0	0
	Bone/joint	66	17	30	17	1	0	1	0
	Central nervous system	13	5	4	1	3	0	0	0
	Lung	156	36	52	54	8	4	2	0
	Other	327	107	134	72	10	4	0	0
	Skin/wound	286	67	97	78	20	16	8	0
	Urine	50	10	27	11	1	1	0	0
Pathogen	Gram-negative	449	108	178	146	15	2	0	0
	Gram-positive	227	62	88	61	10	6	0	0
	Other bacteria	195	60	72	58	5	0	0	0
	Fungus	73	15	24	24	8	1	1	0

Patients may have received more than one infectious code.
* Possible underreporting due to limitations described in the Discussion section.

TABLE 4. Infectious ICD-9 Coding by Pathogen

Syndrome	Code	Code Description	N
Fungus	112	Candidiasis of mouth	7
	112.1	Vulva/vaginal candidiasis	3
	112.3	Candidiasis of skin/nails	2
	112.5	Disseminated candidiasis	4
	112.89	Candidiasis site nec	6
	112.9	Candidiasis site unspec	20
	117.3	Aspergillosis	15
	117.9	Mycoses	16
Gram-negative	041.3	*Klebsiella* infect nos	1
	041.7	*Pseudomonas* infect unspec	7
	041.85	Infection Gram Neg OT	2
	3.8	Other *Salmonella* infections	1
	38.42	*Escherichia coli* septicemia	1
	38.43	*Pseudomonas* septicemia	2
	38.49	Gram-neg septicemia nec	2
	41.3	*Klebsiella* infection nos	90
	41.4	*E. coli* infection nos	43
	41.6	*Proteus* infection unspec	3
	41.7	*Pseudomonas* infection unspec	97
	41.85	Infection Gram negative OT	168
	482	*Klebsiella pneumoniae* pneumonia	14
	482.1	Pseudomonal pneumonia	6
	482.82	*E. coli* pneumonia	1
	482.83	Gram negative pneumonia OT	9
	8	Enteritis *E. coli* unspec	2
Gram-positive	041.02	Infection *Streptococcus* group B	1
	041.11	*Staphylococcus aureus*	5
	041.19	Infection *Staphylococcus* OT	1
	38	Streptococcal septicemia	1
	38.11	*S. aureus* septicemia	4
	38.19	*Staphylococcus* septicemia OT	3
	40	GAS	1
	41	*Streptococcus* unspec	5
	41.01	Infection *Streptococcus* group A	2
	41.02	Infection *Streptococcus* group B	1
	41.03	Infection *Streptococcus* group C	1
	41.04	*Enterococcus* group D	41
	41.09	Other *Streptococcus*	4
	41.1	*Staphylococcus* unspec	47
	41.11	*S. aureus*	66
	41.19	Infection *Staphylococcus* OT	26
	481	Pneumococcal pneumonia	11
	482.3	*Streptococcus pneumonia* unspec	1
	482.31	Group A *Streptococcus* pneumonia	1
	482.4	Staphylococcal pneumonia nos	3
	482.41	Pneumonia *S. aureus*	2
Other bacteria	041.89	Other specified bacteria	7
	32.89	Other specified diphtheria	1
	41.82	*Bacteroides fragilis* infection	2
	41.83	*Clostridium perfringens* infection	1
	41.84	Other anaerobes	9
	41.89	Other specified bacteria	133
	41.9	Bacterial infection nos	20
	795.39	Other nonspecified positive culture	10
	8.45	*Clostridium difficile* enteritis	11
	V09.0	Penicillin-resistant microorganism	1

TABLE 5. Infection ICD-9 Coding by Anatomical and Clinical Syndrome Based

Syndrome	Code	Code Description	N
Abdomen	567.2	Suppurat peritonitis OT	4
	567.8	Peritonitis OT	3
	567.9	Peritonitis unspec	13
	568	Peritoneal Adheshesions Postop/infection	14
	569.6	Colostomy/enterostomy comp unspec	1
	569.61	Colostomy/enterostomy infect	1
	577	Acute pancreatitis	23
	8	Enteritis *Escherichia coli* unspec	2
Bacteremia	38	Streptococcal septicemia	1
	38.11	*Staphylococcus aureus* septicemia	4
	38.19	*Staphylococcus* septicemia OT	3
	38.42	*E. coli* septicemia	1
	38.43	*Pseudomonas* septicemia	2
	38.49	Gram-negative septicemia nec	2
	38.8	Septicemia OT	2
	38.9	Septicemia nos	11
	790.7	Bacteremia	85
Bone/joint	730.02	Acute osteomyelitis arm	1
	730.05	Acute osteomyelitis pelvis	4
	730.06	Acute osteomyelitis leg	8
	730.07	Acute osteomyelitis ankle	2
	730.16	Chronic osteomyelitis leg	3
	730.22	Osteomyelitis unspec arm	3
	730.23	Osteomyelitis unspec forearm	4
	730.25	Osteomyelitis unspec pelvis	6
	730.26	Osteomyelitis nos-L/leg	8
	730.27	Osteomyelitis unspec ankle	4
	730.28	Osteomyelitis unspec OT site	5
	996.66	Infection joint prosthes	2
	996.67	Infection orthopedic device OT	16
Central nervous system	320.89	Meningitis other spec bact	1
	320.9	Bacterial meningitis unspec	6
	322.9	Meningitis unspec	6
Lung	465.9	Acute URI nos	6
	481	Pneumococcal pneumonia	11
	482	*Klebsiella pneumoniae* pneumonia	14
	482.1	Pseudomonal pneumonia	6
	482.31	Group A Strep pneumonia	1
	482.4	*Staphylococcal pneumonia* nos	3
	482.41	Pneumonia *S. aureus*	2
	482.82	*E. coli* pneumonia	1
	482.83	Gram negative pneumonia OT	9
	482.89	Bacterial pneumonia OT	12
	486	Pneumonia, organism nos	75
	510	Empyema with fistula	3
	510.9	Empyema w/o fistula	10
	513	Abscess of lung	2
	V46.1	Dependence on respirator	1
Other	041.89	Infection bacteria OT	7
	112.1	Vulva/vaginal candidiasis	3
	320.9	Bacterial meningitis nos	6
	381.4	Nonsuppurative otitis media unspec	5
	41.89	Infection bacteria OT	133

TABLE 5. Infection ICD-9 Coding by Anatomical and Clinical Syndrome Based (continued)

Syndrome	Code	Code Description	N
	420.9	Acute pericarditis unspec	4
	451.82	Superficl phlebitis arm	4
	451.83	Deep phlebitis arm	1
	451.89	Thrombophlebitis OT	4
	451.9	Thrombophlebitis nos	4
	519.2	Mediastinitis	1
	604	Orchitis with abscess	1
	910.5	Insect bite head infection	2
	98	Acute GC infect lower GU	7
	995.9	SIRS, unsp	5
	995.91	SIRS infection w/o organ dysfun	9
	995.92	SIRS infection w/organ dysfunc	9
	996.6	Infection due to device unspec	2
	996.62	Infection due to vascular device	28
	996.69	Infection due to device OT	4
	998.59	Other postoperative infection	88
Skin/wound	519.01	Tracheostomy infection	1
	528.3	Cellulitis/abscess mouth	1
	566	Anal/rectal abscess	1
	682	Cellulitis/abscess face	10
	682.1	Cellulitis/abscess neck	1
	682.2	Cellulitis trunk	13
	682.3	Cellulitis arm	29
	682.4	Cellulitis hand	14
	682.5	Cellulitis/abscess buttock	3
	682.6	Cellulitis leg	56
	682.7	Cellulitis foot	24
	682.9	Unspec cellulitis/abscess	9
	686.9	Local skin infection unspec	8
	728.86	Necrotizing fasciitis	8
	785.4	Gangrene	10
	912.1	Abrasion shldr/arm infec	1
	916.1	Abrasion hip/leg infection	4
	916.3	Blister hip/leg infection	2
	917.3	Blister foot and toe-infection	5
	958.3	Posttraum wound infection nec	71
	997.62	Infection amputation stump	15
Urine	599	Urinary tract infection nos	40
	788.3	Urinary incontinence nos	10

Nec, not elsewhere classified; nos, not otherwise specified; OT, other; unspec, unspecified; URI, upper respiratory infection; SIRS, systemic inflammatory response syndrome.

Poisson regression directly incorporating each individual's known posttrauma time at risk. Potential within-patient dependence of infectious complications and any resulting extra-Poisson variation were accommodated by estimating a scale parameter (rather than fixing it at 1) to adjust standard errors for over dispersion and mitigate inadvertently increasing the chance of false positive conclusions beyond the targeted 5% level.

RESULTS

We reviewed data from 16,742 patients, 15,021 from Operation Iraqi Freedom (OIF; 9,883 BI, 4,971 non-BI [NBI]) and 1,721 from Operation Enduring Freedom (OEF; 1,090 BI, 599 NBI; Table 1). This represents approximately 70% of the evacuations during the study period. There were 2,703 patient records in 2003, 3,500 in 2004, 2,561 in 2005, 2,711 in 2006, 3,047 in 2007, 1,883 in 2008, and 337 in 2009. The highest number of trauma and infectious ICD-9 codes were from 2003 to 2005 (Table 1), which is consistent with the unavoidable lag in extracting medical records for recent years.

Most patients were male (96.6%) Army personnel (77.6%), 17.9% Marines, and the balance were Air Force and Navy (Table 2). The majority of patients were enlisted (92.6%). The average military ISS ranged from a low of 6.2 in 2003 to a high of 12.5 in 2006. The GCS ranged from 3 to 15 with the highest mean per year of 14.2 in 2003 and a low of 12.7 in 2005. The majority of BI were due to explosive devices while for NBI

TABLE 6. Level of Medical Care at Which Infectious Disease Diagnosis Was Coded

	Level of Medical Care						
	I	II	III	IV	V	Unknown	Total
Clinical and anatomical syndrome	4	10	99	171	446	4	734
Pathogen	0	0	7	157	443	1	608
Other	0	0	1	7	40	0	48

See Ref. 28 for definitions of Level of Medical Care.

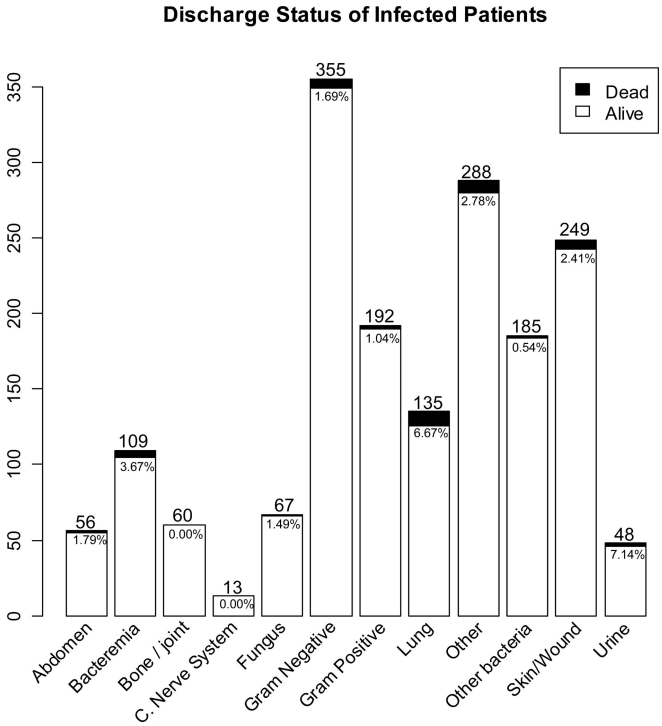

Figure 2. Discharge status of infectious complications among those patients coded as alive or dead with percentage of died with that complication.

motor vehicle crash was most commonly documented (Fig. 1, A and B). The median number of days of hospitalization was 4 with a range of 0 days to 2,196 days. The median number of days requiring mechanical ventilation was 0 with a range of 0 days to 405 days. The median days in the ICU was 1 with a range of 0 days to 337 days (Table 2). Massive transfusions occurred in 768 patients with the highest yearly use in 2006 (Table 2). Individual blood product support, such as red blood cells, fresh frozen plasma and the combination of red blood cells and whole blood, had a higher median use per patient during the later years of the study. The greatest use of transfusions according to combat zone during OIF during 2005 (mean 19.3 units of PRBCs and 2.9 units of whole blood) while in OEF it occurred during early 2008 (mean 15.8 units of PRBCs and 2.2 units of whole blood).

A total of 921 (5.5%) patients had 1 or more infections codes with clear decreases over the study period (Table 2), although this may simply be an artifact of unavoidable lag in the extraction of data from electronic medical records into the JTTR or data extraction concerns. The commonly coded bacteria were gram-negatives (47.6%) and gram-positives (24.0%; Tables 3 and 4). The most common anatomic or clinical syndrome codes were skin/wound infection (26.7%) followed by lung (14.6%; Tables 3 and 5). Infections were diagnosed most frequently at Level V facilities (66.8%; Table 6). There were 111 deaths of which 16 (14%) were infected (Fig. 2). Injury patterns as quantified by MAIS reveal that patients with injuries to the pelvis and external soft tissue had the highest number of infections (Table 7).

Numerous risk factors associated with infection on univariate analysis were present including BI, ISS, body region injured, OEF versus OIF, year of injury, GCS, transfusions, along with ICU, ventilator, and hospital days (Tables 8 and 9 for odds ratios and incidence density rate ratios, respectively). On multivariate analysis, year of injury, mechanism of injury, increasing ISS, and injury pattern were associated with infections. Association with infection on multivariate analysis held true for incidence density rate of infections per 100 person-days after injury to time of infection (Table 10).

DISCUSSION

Continued emphasis on system wide data pertaining to combat-related injury infections is required to improve the overall outcomes of our casualties. This study expands on the numerous single facility, injury site-specific studies and the only previous evaluation of the JTTR for infection specific outcomes for all entries available. Overall, 5.5% of 16,742 casualties assessed in this study had the presence of an infection. These infections involved primarily skin and wound sites or the lung, with a high rate of bacteremia. As in most combat studies, the primary bacteria were gram-negative. The primary risk factor associated with infections was higher ISS reflective of severity of injury.

As in the wars in Iraq and Afghanistan, along with previous conflicts, extremity injuries have been the most commonly encountered injury pattern. It has been noted that

TABLE 7. Infections Based on Injury Pattern

Infectious Complications Noted/ Injury Pattern (M Body Region) by Operation and Overall	Total Number of Patients With MAIS ≥1	Clinical and Anatomical Syndrome or Pathogen		Clinical and Anatomical Syndrome		Pathogen	
		None	1 or More, n (%)	None	1 or More, n (%)	None	1 or More, n (%)
OEF							
Head/neck	542	535	7 (1.3)	535	7 (1.3)	539	3 (0.6)
Face	319	310	9 (2.9)	313	6 (1.9)	312	7 (2.2)
Thorax	196	188	8 (4.3)	189	7 (3.7)	190	6 (3.2)
Abdomen	178	171	7 (4.1)	174	4 (2.3)	172	6 (3.5)
Extremities	840	812	28 (3.4)	822	18 (2.2)	821	19 (2.3)
External	1,066	1,031	35 (3.4)	1,040	26 (2.5)	1,045	21 (2.0)
OIF							
Head/neck	3,888	3,695	193 (5.2)	3,737	151 (4.0)	3,752	136 (3.6)
Face	2,939	2,738	201 (7.3)	2,801	138 (4.9)	2,787	152 (5.5)
Thorax	1,572	1,400	172 (12.3)	1,453	119 (8.2)	1,447	125 (8.6)
Abdomen	1,664	1,480	184 (12.4)	1,528	136 (8.9)	1,537	127 (8.3)
Extremities	7,454	6,931	523 (7.5)	7,143	311 (4.4)	7,062	392 (5.6)
External	9,879	9,192	687 (7.5)	9,427	452 (4.8)	9,410	469 (5.0)
Overall							
Head/neck	4,430	4,230	200 (4.7)	4,272	158 (3.7)	4,291	139 (3.2)
Face	3,258	3,048	210 (6.9)	3,114	144 (4.6)	3,099	159 (5.1)
Thorax	1,768	1,588	180 (11.3)	1,642	126 (7.7)	1,637	131 (8.0)
Abdomen	1,842	1,651	191 (11.6)	1,702	140 (8.2)	1,709	133 (7.8)
Extremities	8,294	7,743	551 (7.1)	7,965	329 (4.1)	7,883	411 (5.2)
External	10,945	10,223	722 (7.1)	10,467	478 (4.6)	10,455	490 (4.7)

TABLE 8. Univariate Analysis of Risk Factors Associated With Development of an Infection (Logistic Regression Using 1 or More Terms Included to Estimate the Overall Effect of Each Predictor)

Risk Factor	N	Comparison	Odds Ratio	95% Confidence Interval	*p*
ISS/MAIS	13,310	Head/neck vs. not	0.20	0.12–0.33	<0.001
Body region	95,41	Extremity vs. not	0.53	0.37–0.76	<0.001
	15,011	Face vs. not	1.17	0.95–1.43	0.13
	14,732	Thorax vs. not	0.94	0.38–2.32	0.90
	14,871	Abdomen vs. not	1.15	0.71–1.87	0.56
	14,955	External vs. not	2.08	1.74–2.49	<0.001
Age	16,392	Age (1 yr increase)	1.01	1.00–1.02	0.35
		18–21 vs. 30–60	0.83	0.69–1.00	0.06
		22–24 vs. 30–60	0.98	0.81–1.17	0.37
		25–29 vs. 30–60	0.91	0.75–1.11	0.79
Gender	16,402	Female vs. male	1.08	0.76–1.55	0.67
Branch of service	16,405	Marine vs. Army	0.56	0.45–0.68	0.54
		Air Force vs. Army	0.47	0.26–0.87	0.32
		Navy vs. Army	0.50	0.28–0.89	0.42
Injury class	16,206	Battle vs. non-battle	2.09	1.77–2.47	<0.001
Military grade/rank	16,296	Officer vs. enlisted	1.04	0.80–1.35	0.78
Disposition	16,405	Dead vs. alive	2.93	1.71–4.99	<0.001
Operation	16,405	OEF vs. OIF	0.44	0.32–0.59	<0.001
MILISS	16,402	MILISS	1.03	1.03–1.03	<0.001
		15–29 vs. low-14	3.71	3.15–4.36	<0.001
		30-high vs. low-14	4.53	3.79–5.40	<0.001
Hospital data	16,251	Hospitalization (d)	1.01	1.01–1.01	<0.001
	15,575	Ventilation (d)	1.19	1.17–1.22	<0.001
	15,725	ICU (d)	1.14	1.12–1.15	<0.001
GCS summaries	13,435	Minimum GCS	0.88	0.86–0.89	<0.001
	16,404	GCS (single imputation of 15 for missing values)	0.87	0.86–0.89	<0.001
Overall* injury pattern	16,277	Head/neck	0.72	0.61–0.85	<0.001
		Face	1.17	0.99–1.38	<0.001
		Thorax	1.86	1.55–2.23	0.065
		Abdomen	1.94	1.63–2.31	<0.001
		Extremity	1.78	1.55–2.05	<0.001
		External/burn/other	2.45	2.05–2.93	<0.001
Blood transfusion	2,150	RBC (unit increase)	1.01	1.00–1.02	0.08
		PLT (unit increase)	0.97	0.91–1.04	0.45
		CRYO (unit increase)	1.10	0.99–1.22	0.08
		WB (unit increase)	1.03	1.01–1.06	0.01
		Plasma (unit increase)	1.00	0.98–1.01	0.79
		RBC + WB (unit increase)	1.01	1.00–1.02	0.02
Massive transfusion	2,150	Yes vs. no	1.03	0.82–1.30	0.80
Injury year	16,405	2004 vs. 2003	1.13	0.95–1.35	<0.001
		2005 vs. 2003	1.37	1.14–1.66	<0.001
		2006 vs. 2003	0.26	0.20–0.35	0.002
		2007 vs 2003	0.11	0.08–0.17	<0.001
		2008 vs. 2003	0.07	0.04–0.13	<0.001

Massive transfusion, ≥10 units of blood product support; PLT, platelets; CRYO, cryoprecipitate; WB, whole blood.

* Overall injury pattern "univariate" model differs from model in first row by adjusting for all other known injury patterns when estimating the effect of an individual injury pattern (non-zero MAIS body region sub-score).

during OIF/OEF there has been a lower proportion of thoracic wounds than in past conflicts. Of those who suffered a torso injury in this study, there is a relatively higher rate of infectious complications.[13] The approximate 11% infectious complication rate among abdominal and thoracic injured patients was higher than the rates described in the Vietnam war of 3.8% and 6.9%, but similar to other reports from Iraq.[8,19,20]

On multivariate analysis, risk factors associated with infections in this study primarily were year of injury, mech-

TABLE 9. Multivariate Analysis of Risk Factors Associated With Development of an Infection (Multiple Predictors in Logistic Regression Performed on n = 16,169; Missing Data or Lack of Record on Injury Pattern, Intensive Care, Ventilation or Blood Transfusion Presumed to Reflect Record That No Such Trauma or Hospitalization Characteristics Exist)

Risk Factor	Comparison	Odds Ratio	95% Confidence Interval	*p*
Operation/yr of trauma	OIF 2004 vs. OIF 2003	1.43	1.16–1.76	<0.001
	OIF 2005 vs. OIF 2003	1.36	1.09–1.68	0.006
	2006 vs. OIF 2003	7.56	5.49–10.41	<0.001
	2007–2008 vs. OIF 2003	17.74	12.11–25.98	0.001
	OEF 2003–2005 vs. OIF 2003	1.13	0.77–1.67	0.53
	OEF 2006–2008 vs. OIF 2003	1.30	0.65–2.62	0.46
Mechanism of injury	Blast injury vs. GSW	0.92	0.75–1.14	0.46
	Burn vs. GSW	0.65	0.38–1.12	0.12
	Penetrating injury vs. GSW	0.79	0.47–1.33	0.37
	Blunt force injury vs. GSW	1.57	1.20–2.07	0.001
	Other injury vs. GSW	1.36	0.58–3.18	0.48
Injury severity	ISS (unit increase <15)	0.84	0.81–0.86	<0.001
Scale (military, maximum on record across levels of care)	Change in baseline risk, 15–29 vs. <15	0.21	0.10–0.47	<0.001
	Change in unit increase, 15–29 vs. <15	1.15	1.10–1.20	<0.001
	Change in baseline risk, ≥30 vs. <15	0.04	0.02–0.07	<0.001
	Change in unit increase, ≥30 vs. <15	1.20	1.16–1.24	<0.001
Injury pattern	Head/neck	1.95	1.55–2.44	<0.001
	Face	1.27	1.06–1.53	0.01
	Thorax	1.00	0.82–1.23	0.97
	Abdomen	0.96	0.79–1.18	0.71
	Extremity	1.06	0.89–1.27	0.52
	External/burn/other	0.63	0.51–0.77	<0.001
Transfusion	Massive transfusion	0.998	0.997–1.002	0.08
Hospital data	Total hospital days over 5 d (unit increase)	1.86	0.81–4.24	0.14
	ICU stay (1 or more days)	0.999	0.997–1.002	0.74

GSW, gunshot wound.

anism of injury, ISS (especially higher ISS score), length of hospital stays/intervention (ICU admission, ventilation), and injury pattern. Risk factors such as transfusions are likely reflective of injury severity and pattern of injury and perhaps should be considered confounders rather than independent risk factors for infections. Although this is in contrast to other publications from OIF/OEF, overall, these risk factors are consistent with previously published studies.[19,24] Year of injury might be reflective of total number of casualties entered into the JTTR with connected infection outcomes data, or it might be due to inherent limitations of the JTTR system which are addressed below.

Despite this being a very large and broad assessment of infectious complications of a purely US population of combat-related injuries, there remain numerous limitations in the use of these data. As previously described, the JTTR has undergone a series of improvements in data collection and entry since its conception, and it is unclear which records have been completely extracted per year for this study. This might result in discrepancies in data over time, reflective of the different methods of defining infection that we implemented in our previous review of the JTTR infectious complications.[24] Also, the collection of Level V data has been incomplete at many facilities. Unfortunately, this is evident by the lack of outcome data for the majority of casualties and not likely reflective of the decreasing infection rate or improvements in infection prevention. This lack of late complication data might miss the importance of gram-positive, notable methicillin-resistant *Staphylococcus aureus*, in infections and place a greater importance on gram-negative early infections. This fact also might indirectly cause systematic data capture errors due to a focus on certain clinical records (i.e., more severe trauma patients) being extracted first lending to the possibility of bias in the data and the higher infection rates noted in the first review of the JTTR. Although the JTTR is designed as a DoD process, the JTTR has not consistently captured Level V Navy and Air Force facilities. A major improvement of the latest version of the JTTR is the implementation of a specific infectious disease module to enhance infectious disease specific data collection, which has been collecting data since June 2009. This ID module has been used by the Infectious Disease Clinical Research Program Trauma Infectious Disease Outcome Study for long-term follow-up of casualties to determine chronic combat-related injury infectious complications. These new projects should overcome the ICD-9 code limitations that prevent granularity, including the ability to capture infections with *Acinetobacter* or methicillin-resistant *Staphylococcus aureus*; pathogens which do not have unique ICD-9 codes. These improvements should also overcome the issue with

TABLE 10. Time Since Trauma Adjusted Multivariate Analysis of Risk Factors Associated With Incidence Density Rate of Infections per 100 Person-Days (Multiple Predictors in Poisson Regression Incorporating Time Since Trauma Across Levels of Care, Performed on n = 16,169; Missing Data or Lack of Record on Injury Pattern, Intensive Care, Ventilation or Blood Transfusion Presumed to Reflect Record That no Such Trauma or Hospitalization Characteristics Exist)

Risk Factor	Comparison	Incidence Density Rate* Ratio	95% Confidence Interval	*p*
Operation/yr of trauma	OIF 2004–2005 vs. OIF 2003	0.82	0.70–0.96	0.02
	OIF 2006 vs. OIF 2003	0.33	0.24–0.45	<0.001
	OIF 2007–2008 vs. OIF 2003	0.13	0.09–0.19	<0.001
	OEF 2003–2008 vs. OIF 2003	0.72	0.52–0.98	0.038
Mechanism of injury	Blast injury vs. GSW	1.01	0.83–1.22	0.96
	Burn vs. GSW	0.81	0.47–1.39	0.44
	Penetrating injury vs. GSW	1.36	0.75–2.46	0.31
	Blunt force injury vs. GSW	0.74	0.57–0.95	0.02
	Other injury vs. GSW	1.13	0.46–2.75	0.80
*ISS	ISS (unit increase, <15)	1.08	1.05–1.11	<0.001
Military	Change in baseline risk, 15–29 vs. <15	1.85	0.95–3.59	0.07
	Change in unit increase, 15–29 vs. <15	0.94	0.91–0.98	0.003
	Change in baseline risk, ≥30 vs. <15	3.69	2.24–6.07	<0.001
	Change in unit increase, ≥30 vs. <15	0.93	0.90–0.95	<0.001
Injury pattern	Head/neck	0.79	0.65–0.95	0.01
	Face	0.91	0.78–1.07	0.25
	Thorax	1.10	0.93–1.29	0.28
	Abdomen	1.01	0.85–1.19	0.92
	Extremity	0.88	0.76–1.03	0.11
	External/burn/other	1.31	1.09–1.59	0.005
Transfusion	Massive transfusion	1.20	0.98–1.46	0.08
Hospital data	Total hospital days over 5 d (unit increase)	0.995	0.994–0.996	<0.001
	Total days in ICU (unit increase)	1.006	1.003–1.009	<0.001
	Ventilator use (1 or more days)	1.49	1.25–1.77	<0.001

GSW, gunshot wound.
* Maximum on record across levels of care.

connecting specific infections with body sites as it is unclear whether those with thoracic injuries are sicker with more infections or whether the infections are involving the thoracic injury itself.

This review of the JTTR provides an ongoing assessment of the challenges facing healthcare providers to control the acute and chronic infectious complications of combat casualties even though the numbers are likely an underrepresentation given the issues with Level V data collection during the study period and the lack of long-term follow-up. There are a number of limitations of the current registry that are actively being addressed through infectious disease specific data collection and analysis. Despite these limitations, these data do enable improvements in ongoing data collection. In addition, they allow for continued focus on developing improvements in patient care and future research programs. Understanding the entire combat-related injury infection epidemiology is the first step toward an evidence-based intervention program.

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